REMARKS

Claims 1, 2, 4-7, 11, 12 and 14-17 are pending in the instant application. Claims 1, 2 and 4-7 have been withdrawn from consideration by the Examiner. Claims 11, 12 and 14-17 have been rejected. Claims 1 and 11 have been amended. New claim 18 has been added. Support for this amendment is provided in the specification, for example, at page 8, lines 12-16. No new matter is added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Restriction Requirement

The Examiner maintained the Restriction Requirement mailed February 22, 2008. Amendments to claim 1 to define the technical feature were deemed unpersuasive as the Examiner suggests that no size limit for the linear peptides is recited and 13 mer peptides spanning the HPA1 mutation are known in the prior art as demonstrated by Flug et al.

Applicants respectfully traverse further maintenance of this Restriction Requirement.

Amendment of the claim to recite a linear peptide is sufficient to distinguish the present claimed invention from the polypeptides of Bowditch comprising conformational epitopes which rely on their tertiary structure for

recognition (see col. 7, lines 24 to 31 of Bowditch). A size limitation is not required.

Further, Applicants respectfully disagree with the Examiner's characterization of Applicants' amendment made to define the technical feature. The Examiner suggests that Applicants argued as part of the December 2, 2009 response that the amendments to the independent claims to recite "linear peptide fragment of a human platelet antigen" defines the technical features. However, the argument made in the December 2, 2009 response was that claim 1 was amended to recite "the composition comprising **an immunologically effective** linear peptide fragment of a platelet protein" (emphasis added). Applicants' argument is consistent with those made in the response to the Restriction Requirement filed April 22, 2008 wherein Applicants stated that "the present invention relates to immunologically effective platelet proteins or peptide fragments useful in preventing or managing a condition caused by exposure to an antithetical allele of a platelet by tolerization and methods for preventing or managing such a condition by tolerization using these platelet proteins or peptide fragments." It is these immunologically effective

platelet proteins or peptide fragments that is the special technical feature linking Groups I and II.

Flug et al. does not teach or suggest the 13 mer peptides to be immunologically effective. Further, claim 1 recites that the immunologically effective linear peptide fragment of a human platelet antigen (HPA) is formulated for delivery through non-invasive routes, a limitation neither taught or suggested by Flug et al.

Accordingly, reconsideration and rejoinder of claims 1, 2 and 4-7 is respectfully requested.

II. Rejection of Claims 11, 12 and 14-17 under 35 U.S.C. 112, first paragraph - Lack of Enablement

The rejection of claims 11, 12 and 14-17 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, has been maintained.

Applicants respectfully traverse this rejection.

At the outset, it is respectfully pointed out that new claim 18 has been added which recites a method for stimulating proliferation of peripheral blood mononuclear cells in a subject, said method comprising administering to the subject an immunologically effective linear peptide fragment of a human platelet antigen (HPA). Enabling support and clear written description for this claim is

provided in the specification at, for example, page 8, lines 12-16, as well as the experiments described beginning at page 11.

Further, the test for enablement is set forth in MPEP 2164.01. Therein, it is stated that "any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable **one skilled in the pertinent art** to make and use the claimed invention." (emphasis added).

In an earnest effort to advance the prosecution of this case and to demonstrate how the instant specification enables one skilled in the art to make and use the instant claimed invention, Applicants are providing herewith a Declaration by Dr. Mark Peakman. Clear from paragraphs 1 through 3 of Dr. Peakman's Declaration, as well as his attached Curriculum vitae, is that Dr. Peakman is skilled in the pertinent art having obtained his PhD in immunology (see paragraph 1 of Dr. Peakman's Declaration) and currently teaching and participating in research in this field (see paragraph 2 of Dr. Peakman's Declaration). Dr. Peakman has worked in the area of immunology and vaccine development for

22 years and is very familiar with the types of experiments performed to demonstrate effective immune responses. See paragraph 3 of Dr. Peakman's Declaration.

Dr. Peakman has reviewed the instant patent application as well as the Office Action mailed March 2, 2010. See paragraph 4 of Dr. Peakman's Declaration.

Dr. Peakman believes the patent application provides sufficient experimental data indicative of tolerization in patients and/or an immunization strategy expected to be effective in preventing or treating conditions such as fetomaternal alloimmune response thrombocytopenia, post-transfusion purpura and platelet refractoriness. See paragraph 5 of Dr. Peakman's Declaration. In particular, Dr. Peakman advises that data presented in Figures 3, 5 and 8 relating to stimulation of PBMCs is predictive of tolerogenic effect in vivo. See Paragraph 5 of Dr. Peakman's Declarations. Thus, experiments presented in the instant specification relating to stimulating PBMCs clearly constitute a working example of the claimed invention to the skilled artisan. See MPEP 2164.02.

A number of references have been cited which are suggested by the Examiner to document that "attempts to induce tolerance in humans have been completely unsuccessful."

Dr. Peakman was provided with copies of the references cited by the Examiner. Dr. Peakman states that these references "are only a selective part of the picture." See paragraph 6 of Dr. Peakman's Declaration. Further in paragraph 6, Dr. Peakman states that "this is a developing field and there are some successes, some partial successes and some failures. As an example, the Examiner provided on PAIR a 2005 reference by Skyler et al. from Diabetes Care 26:1630-1635. In paragraph 6 of his Declaration, Dr. Peakman advises that this 2005 Skyler references describes a therapy that was never intended to be used for tolerance, and so is irrelevant. Indeed Dr. Peakman believed that this may not have been the intended reference. Instead, Dr. Peakman believes more relevant is Skyler et al. 2005 Diabetes Care 28:1068-1076, which he advises in paragraph 6 of his Declaration "IS relevant and shows a beneficial effect of oral antigen in an autoimmune disease." Dr. Peakman advises in paragraph 6 of his Declaration that especially figures 4 and 5 of Skyler et al. 2005 Diabetes Care 28:1068-1076, show that a sub-group of subjects at risk of type 1 diabetes and who have high levels of insulin autoantibodies show delayed progression to disease when given daily oral insulin. Further evidence of tolerogenic effects of antigen in Type 1 diabetes come from the effects

of GAD65 administration (Ludvigsson) and administration of a proinsulin peptide (Thrower). Copies of Skyler et al. 2005 Diabetes Care 28:1068-1076, Ludvigsson and Thrower are provided with Dr. Peakman's Declaration.

The Examiner also cites a reference by Kraus and Mayer referring to IBD, which, Dr. Peakman advises, is not an autoimmune or an alloimmune disease. See paragraph 6 of Dr. Peakman's Declaration.

Dr. Peakman further states in paragraph 6 of his Declaration that "the clinical trials referred to in Marketletter [also cited by the Examiner] used myelin (Myloral) and collagen (Collarol) based preparations and were thus very different to the simple, defined peptide antigens, comprising a known polymorphism/epitope, as disclosed in the patent application." Also see paragraph 11 of Dr. Peakman's Declaration wherein he states that "It is probable that choosing the correct antigen and the correct epitope is important. In that sense the applicant is correct in making the case that the fact that the instant disease has a single antigen provides an expectation of success that is greater than that for diseases associated with multiple and/or undefined antigens."

With respect to the Examiner's citation of Dong et al. (1999) for the statement "Even if we have the ideal strategy

to use in humans, the lack of reliable predictable assays for rejection or tolerance still does not allow us to know if a patient is truly tolerant so that immunosuppressive agents may be withdrawn", Dr. Peakman advises that "there have been major advances in tolerance assays and the identification of tolerance signatures (see for example back to back papers in 2010 June 1st issue of Journal of Clinical Investigation)." See paragraph 6 of Dr. Peakman's Declaration.

Finally, with respect to WO 02/053092, Goodnow (2001) and Bell (2008), which are also cited by the Examiner, Dr. Peakman advises that these are opinions but do not detract from the example of tolerance induction in a complex autoimmune disease using oral insulin and GAD65 as demonstrated by Skyler et al. 2005, Ludvigsson and Thrower. See paragraph 6 of Dr. Peakman's Declaration.

Dr. Peakman advises in paragraph 6 of his Declaration that there have been successes in the field of allergy and liver transplantation as well. These additional successes are discussed in paragraph 10 of Dr. Peakman's Declaration. Therein he states that "the problem of tolerization is not always insurmountable, there have been notable successes, for example, in the field of allergy and in renal

transplantation". As evidence of these successes Dr, Peakman has provided copies of the following references:

Newell et al. J Clin Invest. 2010 Jun 1;120(6):1836-47;

Campbell et al. J Exp Med. 2009 Jul 6;206(7):1535-47;

and

Kamphuis et al. Lancet. 2005 Jul 2-8;366(9479):50-6.

Clearly, the art when viewed in its entirety, provides examples of multiple successful attempts to induce tolerance in humans thus negating the Examiner's suggestion that "attempts to induce tolerance in humans have been completely unsuccessful." This evidence, as well as paragraph 9 of Dr. Peakman's Declaration wherein he addresses reasonableness, or rather lack thereof, of the argument presented by the Examiner regarding an "underlying genetic susceptibility" of these patients in that they have "the wrong GPIIIa allele as compared to the administered blood product" further negate the Examiner's suggestion at page 8 that "problems with tolerization are universally applicable to all disease states."

With respect to concerns raised by the Examiner at pages 6 and 7 regarding the term "tolerance," Applicants believe its meaning is clear when read in light of the experimental data set forth in the specification. Dr. Peakman clearly agrees. See paragraph 7 of Dr. Peakman's

Declaration. However, since the endpoint of prevention or management of a condition caused by exposure to an antithetical allele of a platelet by transfusion or during pregnancy is already recited in claim 11 and is enabled by data presented in the specification (see paragraph 5 of Dr. Peakman's Declaration), and the steps by which this is accomplished are set forth in claim 11, Applicants have deleted the phrase "by tolerisation", thus rendering moot this issue. Claim 1 has been amended similarly.

With respect to further concerns raised by the Examiner at page 7 of the Office Action regarding guidance concerning dosing, MPEP 2164.01(c) is clear; it is not necessary to specify the dosage or method of use if it is known to one skilled in the art that such information could be obtained without undue experimentation. If one skilled in the art, based on knowledge of compounds having similar physiological or biological activity, would be able to discern an appropriate dosage or method of use without undue experimentation, this would be sufficient to satisfy 35 U.S.C. 112, first paragraph. Dr. Peakman addresses the Examiner's concern in paragraph 8 of his Declaration. Therein he states that "the literature provides guidance for dosing regimes." As an example, Dr. Peakman points to the Larche work which is cited by the Examiner. This reference

suggests 1-10 mcg. Dr. Peakman also points to the Thrower reference provided with his Declaration. Clearly, since the literature provides guidance for dosing regimes, further details in the specification are not needed to meet the requirements of 35 U.S.C. 112, first paragraph. See MPEP 2164.01(c).

Finally, with respect to the Examiner's concern that data relating to recognition of epitopes by regulatory T cells has not been provided, Dr. Peakman advises in paragraph 12 of his Declaration that such data showing regulatory responses is not required. Dr. Peakman states that "These are clearly going to be potentially lacking in the disease state, and therefore difficult to demonstrate. Although effector and regulatory T cells can see the same epitope, it does not follow that they must." See paragraph 12 of Dr. Peakman's Declaration. Further, Dr. Peakman's disagrees with the Examiner that that elaboration of additional antibodies through an IgG response would be counterproductive. See paragraph 13 of Dr. Peakman's Declaration. Instead, Dr. Peakman advises that induction of IgG4 is associated with successful induction of immune regulation and operational tolerance in the setting of allergy and there is no reason to suppose it would not be

relevant here. See paragraph 13 of Dr. Peakman's Declaration.

MPEP 2164.02 is clear; the examiner must weigh all the evidence for and against correlation and decide whether one skilled in the art would accept the model as reasonably correlating to the condition. *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (reversing the PTO decision based on finding that *in vitro* data did not support *in vivo* applications).

Paragraph 5 of Dr. Peakman's Declaration makes clear that one skilled in the art accepts the experiments presented in the specification as reasonably correlating to tolerogenic effect in vivo and/or an immunization strategy expected to be effective in preventing or treating conditions such as fetomaternal alloimmune response thrombocytopenia, post-transfusion purpura and platelet refractoriness. Paragraph 6 of Dr. Peakman's Declaration makes clear that evidence presented by the Examiner represents an incomplete picture. Further evidence provided by Dr. Peakman with his Declaration and discussed in detail in paragraphs 6 and 10 of his Declaration makes clear that, contrary to the Examiner's suggestion, attempts to induce tolerance in humans have been successful. As stated by Dr.

Peakman in his Declaration at paragraph 11, "the fact that the instant disease has a single antigen provides an expectation of success that is greater than that for diseases associated with multiple and/or undefined antigens." Finally, as made clear by Dr. Peakman's Declaration in, for example, paragraphs 7, 8 and 12, the skilled artisan does not require the details, guidance and/or data in the specification which the Examiner suggests are needed for enablement. Nor are the rationales presented by the Examiner in the Office Action to question predictability relevant to one skilled in the art with respect to the instant claimed invention. See paragraphs 9, 10, 11 and 13 of Dr. Peakman's Declaration.

When the Examiner weighs all the evidence of record as required by MPEP 2164.02, it is clear that one skilled in the art would accept the data in the specification as reasonably correlating to an immunization strategy expected to be effective in preventing or treating conditions caused by exposure to an antithetical allele of a platelet by transfusion or during pregnancy as claimed. Further, the evidence of record makes clear that adequate guidance is provided by the instant specification to the skilled artisan to make and use the instant claimed invention. Accordingly, the evidence of record, when viewed as a whole, demonstrates

that the instant specification clearly meets the enablement requirements of 35 U.S.C. 112, first paragraph.

Withdrawal of this rejection is respectfully requested.

III. Obviousness-type double patenting rejection

Claims 11, 12 and 14-17 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-22 of copending Application No. 12/096,092.

Applicants respectfully traverse this rejection.

MPEP §804(I)(B)(1) states "[i]f a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer."

Applicants believe that the amendments and arguments of this response overcome all other pending rejections.

Therefore, since the filing or 371(c) date of the instant application precedes the filing or 371(c) date for U.S. Application Serial No. 12/096,092, Applicants respectfully request in accordance with MPEP §804(I)(B)(1)

that the Examiner withdraw this rejection based on the later-filed application.

IV. Rejection of Claims 11, 12, 14, 15 and 17 under 35 U.S.C. 112, first paragraph - Written Description

Claims 11, 12, 14, 15 and 17 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner suggests that amendment of the claims to recite a linear peptide introduces new matter because the length of the peptide is not specified.

Applicants respectfully traverse this rejection.

At the outset, it is respectfully pointed out that page 7, line 31 was provided as an example of where written support for the term linear peptides is provided in the specification. Further support for this term, without an exemplary length of 15 mer, is provided in the written description at page 7, lines 21-25.

The courts have described the essential question to be addressed in a written description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what

is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). MPEP 2163 and the case law also state that if a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See e.g. Vas-Cath, 935 F.2d at 1563, 19USPQ2d at 1116; Martin v. Johnson, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972)(stating "the description

need not be in *ipsis verbis* [i.e., "in the same words"] to be sufficient").

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants are providing herewith a Declaration by Dr. Mark Peakman. Clear from paragraphs 1 through 3 of Dr. Peakman's Declaration as well as his attached Curriculum vitae is that Dr. Peakman is skilled in the area of immunology and vaccine development. Dr. Peakman reviewed the instant patent application. See paragraph 4 of Dr. Peakman's Declaration. After reading the patent application, Dr. Peakman understood that 15-mer peptides inclusive of regions of interest were used in initial experiments because of scale, cost and expediency. See paragraph 14 of Dr. Peakman's Declaration. However, clear from Dr. Peakman's Declaration is that once these were found, it is simply a matter of routine experiments to identify further useful peptides comprising the polymorphism (antithetical allele), as set out in the patent application. See paragraph 14 of Dr. Peakman's Declaration. In support of the types of routine experiments performed to identify further useful peptides, Dr. Peakman has provided with his Declaration copies the following references:

Carson et al. Immunity 1997 Sep;7(3):387-99; and

Carson et al. Immunity 1997 Sep;7(3):387-99; and

Vignali DA, Strominger JL. J Exp Med. 1994 Jun 1;179(6):1945-56.

Accordingly, further length limitations in the instant claims should not be required to meet the written description requirements of 35 U.S.C. 112, first paragraph.

Withdrawal of this rejection is respectfully requested.

V. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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